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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/050,249	03/30/1998	HARUKI OKAMURA	OKAMURA=2B	6601

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EXAMINER	
JIANG, DONG	
ART UNIT	PAPER NUMBER
1646	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/050,249	OKAMURA ET AL.	
	Examiner	Art Unit	
	DONG JIANG	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 April 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *93,95 and 98-120* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *93,95 and 98-120* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED OFFICE ACTION

The request filed on 28 April 2008 for a Continued Examination (RCE) under 37 CFR 1.114 based on parent Application No. 09/050,249 is acceptable, and a RCE has been established. An action on the RCE follows.

Applicant's response filed on 28 April 2008 is acknowledged and entered. Following the amendment, claims 93 and 118 are amended.

Currently, claims 93, 95 and 98-120 are pending and under consideration.

Rejections Over Prior Art:

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 93, 95 and 98-120 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Nakamura *et al.* (*Infect. Immun.* 61: 64-70, 1993), for the reasons set forth in the previous Office Actions.

Applicants argument filed on 28 April 2008 has been fully considered, but is not deemed persuasive for reasons below.

At pages 3-4 of the response, applicants present similar argument as that in the previous responses as that it is considered that Nakamura's factor, even if it comprises the IGIF disclosed one of ordinary skill in the art to obtain monoclonal antibodies to the IGIF alone in Okamura et al. *(Infect. Immun.* 63:3966-3972 1995), is a mixture or a complex which includes a substantial amount of proteins other than IGIF (MW is 50-55 kDa on SDS-PAGE, and 70-75 kDa on gel filtration), thus, it is believed that it would not have been obvious for using such factor; and that the specific activity of the Nakamura's factor is only 56% (page 66 Table 1) of that of the IGIF of the present invention, indicating that Nakamura's factor comprises 44% (100%-56%) of unpurified proteins other than the IGIF, thus, it is clear that numerous kinds of antibodies would be generated and it would require undue experimentation to identify and isolate an antibody against only IGIF. This argument is not persuasive because, as addressed in the previous Office Actions, *even if* Nakamura's factor were less pure, it is irrelevant because high purity is not required for generating antibodies such as that of the present invention. Further it is noted that Nakamura indeed purified the same IGIF, which is evidenced by the statement "it was further purified to apparent homogeneity by PAGE" (abstract), and by the detailed purification procedures (page 65, the last paragraph to the last paragraph of page 66). Furthermore, the Nakamura reference (*Infect. Immun.* 1995, 63: 3966-3972) states "[T]hus IGIF in the serum sample was proved to be the same IGIF as that found in liver extract, and it was considered to be bound to another protein or to exist in an oligomeric form", indicating that the higher MW substance comprised either just one protein (in an oligomeric form), or two proteins (IGIF and "another protein"), not "a substantial amount of proteins" as alleged by applicants. Such purity of the protein would be sufficient for generating antibodies. Given the established technology in making antibodies and monoclonal antibodies, and the teachings of Nakamura (the factor, purification and the specific activity), one of ordinary skill in the art would be able to obtain monoclonal antibodies to the IGIF. Furthermore, applicants calculation of 44% of unpurified proteins other than the IGIF in Nakamura's purification based on specific activity is irrational because specific activity may vary depending on many factors such as purification procedures, and experimental variations. For example, a highly purified protein preparation may not necessarily have higher specific activity among different purifications, due to reasons other than

purity, such as denatured protein. Prior art has never established that less specific activity equals to the amount of unpurified other proteins. As such, applicants argument is unsound.

At pages 4-5 of the response, applicants present similar argument as that the antibody of the present invention is not an antibody obtained by using Nakamura's factor, but an antibody obtainable by using the IGIF having a specific activity of about 5 x 10^5 units/mg protein, that, even though Nakamura's factor comprises the IGIF, it would have been difficult to expect with a reasonable expectation of success that the antibody of the present invention is obtained by using Nakamura's factor without undue experimentation. Applicants further argue that the difference in purity is an important matter influencing the possibility of success in obtaining antibodies against the IGIF of the present invention. This argument is not persuasive because, as addressed above, Nakamura has purified the same IGIF, and a specific activity has less to do with antigenicity, i.e., a protein with 100% purity may not have a specific activity (due to, for example, denature of the protein), and maintain its antigenicity. *Even if* Nakamura's factor were less pure than that of the present invention, screening additional clones would not be considered undue experimentation as the technology has been well established and widely practiced in the field with great success, and was considered routine and conventional experimentation.

At pages 5-6 of the response, applicants repeatedly argue that Nakamura's factor losing activity after SDS-PAGE, and the IGIF of the present invention does not lose its activity by the use of reducing agent, that Okamura also states at page 3969, left column, second paragraph, that IGIF does not lose its activity by the use of reducing agent, indicating that Nakamura's factor is a different substance from IGIF. This argument is not persuasive because Okamura also states at page 3969, left column, second paragraph (middle), that "the activity was observed *only* in the molecular species of 75-80 kDa *without* DTT" (also see Figure 5). Further, as repeated by the examiner, Okamura clearly states "[T]hus IGIF in the serum sample was *proved* to be the same IGIF as that found in liver extract". Therefore, there is no doubt that Nakamura's factor is the same substance as the IGIF of the present invention.

At pages 6-7 of the response, applicants argue, citing the Sevier and Lochner references, that whether a desired antibody is obtainable depends on the purity of an antigen; that it is apparent that IGIF with high purity is required as an antigen in order to obtain an antibody

against IGIF; and that Nakamura never obtained antibodies against IGIF, and no prior art is cited and applied that discloses antibodies against IGIF, accordingly, Nakamura does not and cannot make obvious the presently claimed invention. This argument is not persuasive because, as addressed above and previously, Nakamura has purified the factor to a significantly high degree, which is evidenced by the statement "it was further purified to apparent *homogeneity* by PAGE" (abstract), and by the detailed purification procedures (page 65, the last paragraph to the last paragraph of page 66, and Table 1). Such purity is clearly sufficient for a protein to serve as an antigen for generating antibodies. Further, there is no specifically high purity is required for generating antibodies. While Sevier indicates that the lower purity of a protein (immunogen) may result in increased screening ("to minimize screening problems when dealing with soluble antigens, the immunogen should be as pure as possible, because the purity of the immunogen may reflect the frequency of positive clones"), the reference does not indicate that the antibody would not be obtainable otherwise. As addressed above, screening additional clones was considered routine and conventional experimentation. With respect to the argument that Nakamura never obtained antibodies against IGIF, and does not and cannot make obvious the presently claimed invention, as addressed previously, the rejection is not anticipating, but obviousness rejection. It would have been obvious to the person of ordinary skill in the art at the time the invention was made to make monoclonal antibodies to Nakamura's factor as the mAbs could be used, at least, for immunoaffinity purification of the protein for the future study of the factor, for example. Also, as discussed previously, Nakamura indicated the necessity of such monoclonal antibodies. The person of ordinary skill in the art would have been motivated to make monoclonal antibodies to Nakamura's factor, and reasonably would have expected success because of the fact that the technology of making monoclonal antibodies was well established, and widely and successfully used in the art at the time the present invention was filed. For example, Boldain et al. (Monoclonal Antibodies For Cancer Detection And Therapy, page 20, 1985, cited previously by the examiner) teaches that it is relatively easy to make additional monoclonal antibodies to an antigen that has already been identified.

Conclusion:

No claim is allowable.

Advisory Information:

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication should be directed to Dong Jiang whose telephone number is 571-272-0872. The examiner can normally be reached on Monday - Friday from 9:30 AM to 7:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, can be reached on 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

/Dong Jiang/
Primary Examiner, Art Unit 1646
7/2/08